



A REVIEW ON PHARMACEUTICAL APPLICATIONS OF TAMARIND SEED POLYSACCHARIDE: A NOVEL GREEN POLYMER

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Abstract : The natural polymers always have exceptional properties which make them distinct from the synthetic polymers and tamarind seed polysaccharide (TSP) is one such example which shows more valuable properties for a wide range of applications. In recent years polysaccharides are used widely in food, cosmetic and pharmaceutical industries. The near future of drug delivery system would lie in the search of a versatile and harmless material, based mostly on the natural resources. The recent use of biopolymers derived from agricultural feed stocks has attracted the attention of many researchers. So, this review mainly focuses on the utility of TSP in pharmaceutical applications.

Index Terms - Tamarind seed polysaccharide, Green polymer, drug delivery, xyloglucan.

INTRODUCTION

Tamarind Seed Polysaccharide:

It is a biodegradable polysaccharide extracted from Tamarind seeds (*Tamarindus indica* Linn. Family; *Leguminosae*) called as TSP. *Tamarindus indica* L., commonly known as tamarind tree, is one of the most important multipurpose tree species in the Indian sub-continent. It is a large evergreen tree with an exceptionally beautiful spreading crown, and is cultivated throughout almost the whole country, except in the Himalayas and western dry regions^[1]. Xyloglucan (XG) is a major structural polysaccharide in the primary cell wall of higher plants. Seeds of the tamarind tree (*Tamarindus indica*) contain a xyloglucan. It is called 'ageing free starch' because its property is similar to starch but is more stable^[2]. Natural polymers such as TSP have advantages over synthetic and semi-synthetic polymers like low cost, natural origin, less side effects, locally available and better patient tolerance. However, these natural substances suffer with the drawbacks like purity, source and microbial contamination. If these factors can be identified and controlled, natural substance can be good substitute for synthetic polymers^[3].

One such cheap and agro-based bio-material is tamarind seed polysaccharide (TSP) obtained from tamarind seed. Natural polysaccharide-based bio-materials are currently being explored as novel drug delivery devices. Important properties of the polysaccharides include controlled biological activity and biodegradability. Development of new excipients is time consuming, involves tedious procedures and is highly expensive. Instead, identification of new uses for the existing substances is relatively inexpensive and less time consuming^[4].

Natural products always take over synthetic ones due to their easy availability, non-toxicity, capability of chemical modifications, potential biodegradability and bio-compatibility property, as compared to the expensive synthetic polymers with environment related issues, long development time for synthesis and toxicity which makes them undesirable^[5]. Now-a-days, natural gums, obtained mainly from seeds or other plant parts, have become a thrust area in majority of investigations in drug delivery systems, switching from the synthetic excipients available in the market. Recent researches show that tamarind gum has become a potential polymer in pharmaceutical industries. The tamarind seed is a by-product of the tamarind industry. The decorticated flour, known as tamarind kernel powder has been tried for various biomedical applications such as drug delivery carriers.

The xyloglucan component of it, a hemicellulose, was found to be a biocompatible, non-toxic and cheap agro-based material that could be used safely for controlled drug delivery systems. TSP, a natural polysaccharide, is recently gaining a wide potential in the field of pharmaceutical and cosmetic industries. Its isolation and characterization involve simple techniques resulting in cost effective yield in its production. TSP shows uniqueness in its high drug holding capacity, high swelling index and high thermal stability, especially necessary for various novel drug delivery systems. It also plays the role of stabilizer, thickener, binder, release retardant, modifier, suspending agent, viscosity enhancer, emulsifying agent, as a carrier for novel drug delivery systems in oral,

buccal, colon, ocular systems, nanofabrication, wound dressing and is also becoming an important part of food, cosmetics, confectionery, textiles and bakery. Various studies and experiments have been carried out to prove its multifunctional potentiality, from which it can be concluded that TSP can be a promising natural polysaccharide having enormous applications. This review focuses on the diverseness of applications of TSP^[6].

1. Pharmaceutical applications

TSP is an interesting candidate for pharmaceutical use. It is used as a carrier for variety of drugs for controlled release applications. Many techniques have been used to manufacture the TSP-based delivery systems, which makes it an exciting and promising excipient for the pharmaceutical industry for the present and future applications.

1.1. Formulation Applications

1.1.1. Binder in tablet dosage form

Evaluations of tamarind seed polyose as a binder for tablet dosage forms was taken up for the wet granulation as well as direct compression methods. The results indicated that tamarind seed polyose could be used as binder for wet granulation and direct compression tableting methods^[7]

1.1.2. As a mucoadhesive polymer

TSP is used for production of thickened ophthalmic solutions having a pseudo plastic rheological behaviour and mucoadhesive properties. The solution is used as artificial tear and as a vehicle for sustained release ophthalmic drugs. TSP is an adhesive thereby prolongs the retention time of formulation onto the surface of eye unlike other eye preparations. Furthermore, the TSP drops did significantly better job of relieving several key subjective symptoms of dry eye syndrome namely trouble blinking, ocular burning, and having sensation of having something in someone's eye^[8]. It also increases the resident time of the drug to the cornea, e.g. α -blockers. The effect of an ophthalmic preparation containing timolol and TSP on intraocular pressure was evaluated in rabbits and found to decrease considerably.

1.1.3. In sustained drug delivery

It is a potential polysaccharide having high drug holding capacity which sustained the release of Verapamil hydrochloride. The release pattern was found to be comparable with matrices of other polysaccharide polymers such as ethyl cellulose, hydroxyethyl cellulose, and hydroxypropylmethyl cellulose, as well as the commercially available sustained release tablets^[9]. Sustained release behaviour of both water-soluble (acetaminophen, caffeine, theophylline and salicylic acid) and water-insoluble (Indomethacin) drugs on TSP was examined. Studies showed that TSP could be used for controlled release of both water-soluble and water insoluble drugs. Zero-order release can be achieved selecting sparingly soluble drugs such as indomethacin along with TSP. The rate of release can be controlled by using suitable diluents such as lactose and microcrystalline cellulose^[10]. For water-soluble drugs, the release amount can also be controlled by partially cross-linking the matrix. The extent of release can be varied by controlling the degree of cross-linking. The mechanism of release due to effect of diluents was found to be anomalous and was due to cross-linking.

1.1.4. In ocular drug delivery

Administration of vicosified preparations produced antibiotic concentrations both in aqueous humor and cornea that were significantly higher than those achieved with the drugs alone. The increased drug absorption and the prolonged drug elimination phase obtained with vicosified formulations indicate the usefulness of the TSP as an ophthalmic delivery system for topical administration of antibiotics. Eye drops from TSP are used to treat dry eye syndrome. TSP was used for ocular delivery of 0.3% rifloxacin in the treatment of experimental *Pseudomonas aeruginosa* and *Staphylococcus aureus* keratitis in rabbits. The polysaccharide significantly increased the intraocular penetration of rifloxacin in both infected and uninfected eyes. Polysaccharide allowed sustained reduction of *S. aureus* in cornea to be achieved even when the time interval between drug administrations was extended. These data suggest that TSP prolongs the precorneal residence time of antibiotic and enhances the

drug accumulation in the cornea, probably by reducing the washout of topically administered drugs.^[10] The concentrations of TSP preferably employed in ophthalmic preparations for use as artificial tears, i.e. products for replacing and stabilizing the natural tear fluid, particularly indicated for the treatment of dry eye syndrome are comprised between 0.7% and 1.5% by weight. The concentrations of tamarind polysaccharides comprised between 1 to 4 % by weight is preferably employed in the production of vehicles (i.e. delivery system) for ophthalmic drugs for prolonging the prevalence time of medicaments at their site of actions^[11].

In controlled release of spheroids TSP was used as release modifier for the preparation of diclofenac sodium spheroids using the extrusion spheronization technique with microcrystalline cellulose as a spheronization enhancer. It was found that release was sustained over a period of 7.5 h⁵⁹. A credible correlation was obtained amongst swelling index, viscosity, and surface roughness of the polysaccharide particles and in vitro dissolution profile of spheroids. In the comparative bio availability study, the developed spheroids have been able to sustain drug release and also were found to improve the extent of absorption and bio availability of drug (e.g. diclofenac sodium, caffeine, etc.)^[12].

1.1.5. Nasal drug delivery

The highly perfused nasal mucosa provides an excellent site for rapid absorption of drugs. The main drawback associated with nasal drug delivery is a rapid mucociliary clearance (MCC) that limits the time available for drug absorption from the applied dosage form^[13]. In the context of the above mentioned problem, thermoreversible in situ mucoadhesive gel formulation is a plausible strategy, which forms a gel at nasal mucosal temperatures. The mucoadhesive polymer lengthens the residence time at the mucosal surface, thereby improves the nasal drug bio availability. Kumar et al.^[14] formulated a thermoreversible in situ mucoadhesive gel for nasal administration of zolmitriptan (ZT) and ketorolac tromethamine (KT) with an objective to improve the bio availability of combinational drugs by increasing the residence time at the nasal mucosal surface. In this study, Box-Behnken experimental design approach has been utilized to assess the influence of various factors on the critical quality attributes of the formulation. In addition, histopathological examination executed on excised sheep nasal mucosal membrane revealed that the formulation was safe for intranasal administration. The statistical difference in the absolute bio availability after oral and intranasal administration suggested that the administration through intranasal route increased the bio availability of ZT and KT by 21 and 16%, respectively. In summary, the authors have concluded that the optimized in situ gel formulation would help to diminish the symptoms associated with migraine much better than the presently available commercial formulation.

1.1.6. Pulmonary drug delivery

The pulmonary delivery of drugs has been investigated widely by the researchers, especially for delivery of proteins, peptides and genes, owing to the merits offered by this route viz. avoidance of hepatic first-pass metabolism, large alveolar surface area available for drug absorption, the low thickness of the epithelial barrier, extensive vascularization and relatively low proteolytic activity in the alveolar space compared to other routes of drug administration [15,16]. The recent advances in the dry-powder inhalation (DPI) technology have addressed some of the limitations associated with inhaled formulations, including unwanted loss of drug due to oropharyngeal deposition [17]. To overcome the unwanted drug loss and poor particle deposition into the lungs, Mahajan & Gundare (2014) [18] proposed a method based on microencapsulation of drug into the polymer to produce polymeric microspheres as DPI. In their study, a novel polymeric microparticles system has been developed using XG as a mucoadhesive polysaccharide, employing the spray drying technique. XG has prolonged the residence time of drug-loaded microspheres into the lungs. Montelukast sodium (MS), an antiasthmatic agent, has been used as a model drug. A 3² factorial design was used to design and optimize the MS-loaded microspheres formulation. The formulations exhibited good entrapment efficiency in the range of 75–90%, good flow properties indicated by the angle of repose between 28–40°, and excellent mucoadhesive strength in the range of 74–91%. Microspheres showed spherical morphology with smooth surface and particle size in the range of 0.9–6 µm, which are supposed to be suitable for inhalational drug delivery. The mass median aerodynamic diameter of the microspheres was found to be 2.53 µm, which is less than 5 µm, and hence suitable for inhalation of powders into lower regions of the lungs. The pulmonary pharmacokinetics executed on Wistar rats confirmed that there is an increase in the bio availability of XG-based microspheres as DPIs compared to plain MS at 6 h after pulmonary administration. This may be credited to the prolonged residence of XG-based microspheres in the lungs.

1.1.7. Rectal drug delivery

The rectal route, though rarely used, is an efficient alternative to oral and parenteral administration of drugs. Rectal administration offers many potential advantages for drug delivery viz. Rapid absorption of many small molecules, partial avoidance of hepatic first-pass metabolism, potential for absorption into the lymphatic system, and retention of large volume of formulation into the rectum [19]. Miyazaki et al. [20] investigated the thermally reversible XG gels as vehicles for rectal drug delivery. Indomethacin and diltiazem were utilized as model drugs. In this study, the authors have compared the in vitro release characteristics of the hydrophobic drug indomethacin from gel formulation of enzyme-degraded XG with those of the more hydrophilic drug diltiazem. In addition, the bio availability of the rectally administered indomethacin loaded XG-based gel was compared with that achieved after rectal administration of the commercially available indomethacin-loaded suppositories. The results of this experiment confirmed that the in vitro release of indomethacin was more sustained from the XG-based gel formulation than from commercial suppositories. Histopathological examination of the rabbit rectal mucosa 6 h after administration of the 2% w/w XG-gels with and without indomethacin revealed no evidence of tissue damage and suggested that the applied gel formulation is safe for rectal administration. Pharmacokinetic studies indicated that there was no significant difference in the bio availability of indomethacin when administered by XG-based gels and commercial suppositories.

1.1.8. Buccal drug delivery

The rapid drug uptake into the systemic circulation and improved bio availability of drugs leading to rapid onset of action are the prominent advantages offered by buccal route among other transmucosal routes [21]. Moreover, buccal drug delivery systems also bypass the hepatic first-pass metabolism by mediating the absorption through the venous system that drains from the cheek [22]. Buccal mucosal membrane also offers several specific advantages viz. rapid and rich blood flow, less thickness of the

buccal mucosa and flexibility of designing unidirectional or multidirectional release systems for local or systemic action [23]. Buccal films, wafers, tablets, and gels have been developed till date, as buccal-adhesive drug delivery devices. Among these, a mucoadhesive buccal film offers several benefits due to its small size, thickness, and improved patient compliance compared to buccal tablets or gels [24]. Avachat et al. [25] developed mucoadhesive buccal films based on XG for systemic delivery of rizatriptan benzoate via buccal route. A 3² factorial design was employed for the preparation and optimization of the formulation. Concentration of XG and carbopol 934P were considered as independent variables while tensile strength, bioadhesive force, and drug release were considered as dependent variables. The data for tensile strength determination revealed that the prepared buccal films have sufficient strength to withstand during transportation and administration. The tensile strength of films was found to be increased with increasing concentrations of glycerin and XG. The XG-based buccal films showed good bioadhesion due to good swelling index. The bioadhesion force was found to be increased with the increase in concentration of XG. The permeation experiment, executed on the excised porcine buccal mucosa, indicated that the buccal films containing 4% w/w XG provided high permeation of drug compared to other formulations. In summary, XG can potentially be explored as a bioadhesive polymer for the development of bioadhesive buccal films for the treatment of migraine.

1.1.9. Oral drug delivery

A variety of polymers have been explored to fabricate gel formulations with suitable characteristics for administration by geriatric patients, particularly those who experiences difficulty in swallowing the more conventional dosage forms such as tablets or capsules. The oral drug administration in the form of gel formulations is an excellent mean of improving patient compliance due to ease of handling, and swallowing, more preferably in elderly patients [26]. Miyazaki et al. [27] have designed gel formulations based on agar, gelatin, gellan, pectin, and XG. The gels were loaded with paracetamol and intended for oral administration. The prepared gel formulations were evaluated for the gel strength determination. The results suggested that the gellan (1.5% w/w) and XG gels (1.5% w/w) had sufficient gel strength. The commercial gel formulation was too soft to be analyzed. The in vitro and in vivo release characteristics of all prepared gels were compared with Kazepitan TM jelly (150 mg/30 g), which contains agar as a gelling agent, and is commercially available in Japan for oral administration of paracetamol [27]. It was observed that the in vitro drug release from the commercial formulation was rapid and complete after 3 h while XG gel released about 75% of the drug in 5 h indicating a more sustained drug release. From in vivo experiment, it was clear that the plasma drug levels following oral administration of paracetamol (5 mg) to Wistar rats from XG gel (1.5% w/w) were more prolonged compared to that from the commercial gel (5 mg in 1 g). In addition, the bioavailability of paracetamol was improved by 1.35 times from the XG-based gel compared to commercial gel [27]. Visual observation of the contents of the stomach after oral administration of XG gel (1.5% w/w) showed the gradual erosion of the gel to about 59% of the administered amount after 3 h, indicating its good integrity in the stomach. A similar erosion rate was

observed for gellan-based gel (1.5% w/w). This may be attributed to the sustained release of paracetamol from these gels. In contrast, only a 9% of a 1.5% w/w pectin gel and 28% of the 0.5% w/w agar gel remained in the stomach after 3 h. A complete disappearance of the 1.5% w/w gelatin gel and commercial gel was observed, may be due to rapid release of paracetamol from these vehicles [27].

1.1.10. Periodontal drug delivery

Periodontitis is a severe gum infection caused by bacteria, which affects the supporting structures of teeth such as gums, periodontal ligaments, alveolar bones, and dental cementum. Periodontitis further leads to progressive loss of alveolar bone round the teeth and thus forms infected pockets between teeth and gums [28,29]. It can be treated by using scaling and root planning, but it needs anaesthesia by painful needle therapy [30]. An useful alternative to this anaesthesia therapy is the application of gels. Though these topical gels are easy to apply, they suffer some drawbacks like lower retention in plaque areas, tendency to spread over other areas, and probability of swallowing of gels. In situ gels shows promising effects in improving the residence time at the site of action due to their increased viscosity, and mucoadhesiveness, thereby exhibits rapid onset of action [31,32]. Pandit et al. [33] prepared the XG-based thermoreversible mucoadhesive in situ gel loaded with lidocaine hydrochloride (LH) for the treatment of periodontitis. A 3² full factorial design tool was employed to optimize the gel formulation. Viscosity study confirmed that there is a marked increase in the viscosity of the gel at 37°C due to sol-to-gel transition. Gelation of the formulation occurred near to the body temperature. XG was observed to be a good mucoadhesive polymer which retains the gel at the site of application in the dental pockets for a prolonged period of time. The prepared gel formulation also exhibited good gel strength, validating the retaining capacity of the gel in the periodontal pockets. The in vitro drug release studies depicted a fast onset of drug action with the release of about 90% drug at 2 h. The in vitro permeation studies executed on the excised oral mucosal tissue of sheep indicated a good permeation of LH (~ 98%) after 2 h. Experimental design assisted optimization suggested a gel formulation containing 1% XG and 18% Lutrol F127 as an optimized sample for periodontal application. In summation, LH-loaded thermoreversible in situ gel offered a workable option to the painful injection therapy during dental surgery.

1.1.11. Parenteral (intraperitoneal) drug delivery

Mitomycin C (MMC), a clinically important antineoplastic antibiotic has been given intraperitoneally (i.p.) in solution form for carcinomatous peritonitis [34]. However, MMC solution get rapidly absorbed into blood plasma, thereby fails to keep sufficient concentration of MMC into the intraperitoneal cavity [35]. In order to overcome this problem, Hagiwara et al. [34] developed MMC adsorbed activated carbon particles as sustained release vehicles. Miyazaki et al. [36] evaluated the potential of Pluronic F127 gel as a sustained release vehicle for i.p. administration of MMC in the treatment of Sarcoma-180 ascites. With an objective to get rid of possible toxicity issues due to use of high concentrations of Pluronic F127 required for gelation, Suisha et al.

[37] examined the potential use of a thermoreversible gel formulation prepared using XG (which forms gel at low concentration) for i.p. administration of MMC. The results of in vitro drug releases studies indicated that the MMC was released slowly from the XG-based gels and followed root-time kinetics over a period of 5 h. MMC-loaded XG-based gels (1.5% w/w) resulted in a broad concentration-time profile both in ascites and in plasma over a period of 3 h, after i.p. administration in Wistar rats. In contrast, a narrow concentration-time profiles and rapid clearance was observed from both the sites when MMC was administered i.p. as a solution.

1.1.12. Transdermal drug delivery

The topical application offers several advantages over oral administration, such as avoidance of hepatic first-pass effects and gastric irritation, while delivering the non-steroidal anti-inflammatory drugs (NSAIDs). Several studies have investigated the potential of Pluronic F127 gel as a vehicle for topical delivery of NSAIDs [38-41]. XG gels have also been explored for rectal [42], intraperitoneal [43], ocular [44], and oral [45] drug delivery. Later, Takahashi et al. [46] compared the potential of XG and Pluronic F127 gels as potential vehicles for the topical delivery of NSAIDs (ibuprofen and ketoprofen), both in vitro and in vivo. It has been found that the chilled aqueous solutions of XG, partially degraded by galactosidase, forms gel at a concentration of 1–2% w/w when warmed at 37°C. Release experiments revealed that the in vitro release of ibuprofen and ketoprofen at pH 7.4 from the XG gels followed root-time kinetics over a period of 12 h after an initial lag time. Both the drugs were released from the XG gels (1.5% w/w) with higher diffusion coefficients as compared to when released from Pluronic F127 gels (25% w/w). This difference in drug release was ascribed to the difference in the structure of the gels. Pluronic F127 forms a cubic gel structure by the packing of the micelles of this triblock copolymer [47] whereas XG forms a thermoreversible gel due to lateral stacking of rod-like chains [48]. The authors also compared the plasma concentrations of ibuprofen and ketoprofen from the XG and Pluronic F127 in situ gels after topical application to the abdominal skin of Wistar rats. It was noted that the bioavailabilities of both ibuprofen and ketoprofen were significantly enhanced when released from XG gels compared to Pluronic F127 gels. In brief, this study demonstrated the potential of XG-based in situ gels as sustained release vehicles for percutaneous application of NSAIDs [46].

1.1.13. Colon targeting

The potential use of TSP as a carrier for colonic drug delivery was demonstrated [49]. Matrix tablets were prepared by wet granulation methods using ibuprofen as a model drug. In vitro release studies mimicking mouth to colon transit demonstrated the ability of TSP to release the drug at pH 6.8. TSP was remarkably degraded in rat colon indicating that TSP can be used as a carrier for colonic drug delivery [50].

1.1.14. Bio-adhesive tablet

Tablets prepared from the TSP and tamarind gum were evaluated as bio-adhesive tablets and was found that the tablets showed longest residence time in oral cavity as compared to that prepared from xanthan gum and carboxycellulose but the unpleasant taste of the former gradually developed.

1.1.15. As a suspending agent

The Tamarind seed polysaccharide (TSP) possesses properties like high viscosity, broad pH tolerance, no carcinogenicity, mucoadhesive nature, and biocompatibility. Since suspensions are thermodynamically unstable, it requires a suspending agent which reduces the rate of settling and permits easy redispersion of any settled particulate matter. R. Deveswaran et.al. has done an attempt to use this polysaccharide as suspending agent in the formulation of Nimesulide suspension. They found that the TSP powder can be used as an effective suspending agent [50-54].

1.2. Pharmacological/Biomedical applications

1.2.1. Antimutagenic activity

Xyloglucan has a number of pharmacokinetic properties^[55-58]. Pronounced antimutagenic effects are found for xyloglucan against 1-nitropyrene induced mutagenicity^[59]. Xyloglucan extracted from tamarind mucilage has been studied for its nontoxic behavior. In a study conducted on B6C3F1 mice, lack of carcinogenicity of tamarind seed polysaccharide was seen. Detailed histopathological examination also revealed no treatment-related increase in the incidence of any non-neoplastic or neoplastic lesions^[56]. Formulating sunscreens with a high SPF, as well as a high immune protection factor, is necessary for preventing skin cancer and maintaining effective immune responses to infectious disease after sun exposure. Supplementing current sun-protection products with immunoprotective compounds may help fill the gap between erythema protection and immunoprotection. Animal and now human studies have shown that a class of agents known as oligosaccharins—complex carbohydrates, particularly XG—protect the cutaneous immune system from UVB-induced and UVA-induced immunomodulation. The ability of XG's poly/oligosaccharides to prevent suppression of T cell-mediated immune responses and suppressor cell induction during chronic ultraviolet irradiation has been investigated. Treatment of keratinocytes with immunoprotective carbohydrate, XG and aloe poly/oligosaccharides reduces IL-10 production by approximately 50% compared with cells treated with UV radiation alone and completely blocks the suppressive activity of the culture supernatants *in vivo*. XG also blocks UV-activated phosphorylation of SAPK/JNK protein but has no effect on p38 phosphorylation. Xyloglucan, when topically applied, inhibits the solar-simulated ultraviolet radiation responses in humans. Carbohydrate, XG and aloe poly/oligosaccharides reduces IL-10 production by approximately 50% compared with cells treated with UV radiation alone and completely blocks the suppressive activity of the culture supernatants *in vivo*. XG also blocks UV-activated phosphorylation of SAPK/JNK protein but has no effect on p38 phosphorylation. Xyloglucan, when topically applied, inhibits the solar-simulated ultraviolet radiation responses in humans^[60-63].

1.2.2. Antiviral activity

Antiviral activity of many natural and semisynthetic polysaccharides on the early steps of rubella virus (RV) infection is known^[64]. Among the many polysaccharides and their semisynthetic derivatives, XG's sulfate derivative (glyloid sulfate 4324) is found to have an inhibitory effect on the initial stages of the rubella virus infection and has the highest inhibitory effect on RV antigen synthesis. XG derivative blocks a step in virus replication subsequent to virus attachment, such as internalization and/or uncoating. XG shows a marked inhibitory effect on BK virus binding to the cells. It is observed that polyanions like mucin, dextran sulfate and heparin depress the viral binding to cell but the results do not appear to be related with the electric charge on the polymer as XG being the neutral compounds^[65].

1.2.3. Antioxidant and Antitumor activity

Two kinds of xyloglucan derivatives (xyloglucan selenious ester and sulfated xyloglucan) were prepared and evaluated for antioxidant activity and antitumor activity. Compared with xyloglucan, xyloglucan derivatives have new bioactivity against oxidative damage and tumor. Furthermore, xyloglucan selenious ester is more potent than sulfated xyloglucan in terms of antioxidant activity and antitumor activity *in vitro*. The current data suggest for the first time that selenization of xyloglucan significantly increases its bioactivity and the chemical modification of polysaccharides may allow the preparation of derivatives with new properties and a variety of applications^[66-69].

1.2.4. As dietary fiber

Xyloglucan oligosaccharides obtained by enzymatic hydrolysis may be applied as a prebiotic food ingredient. Being nonmetabolized, it acts as a soluble food fiber that can increase the viscosity of digesta in the stomach and small intestine to reduce the rate and extent of absorption of nutrients. A dietary fibre would also have an impact on fermentable intestinal bacteria as prebiotics. Enzymatically depolymerised XG oligosaccharides have been used to replace sugar in low calorie food products^[70]. Acceleration of metabolism and excretion of endocrine disrupting chemicals by XG has been reported^[71]. XG as soluble food fiber can be degraded by the intestinal microflora^[72]. The octasaccharide and nonasaccharide obtained from XG may not only serve as a soluble dietary fiber with low molecular weight but also lower the blood sugar level^[73]. It also shows hypolipidemic effects which may be important for the treatment and prevention of geriatric diseases, including diabetes and cardiac disorders^[74]. Human physiological effects show that XG adds viscosity to the small intestine and gets fermented in the human colon^[75]. Xyloglucan oligosaccharides obtained by enzymatic hydrolysis may be applied as a prebiotic food ingredient.

1.2.5. As solid-phase diagnostics

One of the applications of polysaccharides in the biomedical field is their use in the formation of nanoporous matrices on solid supports, which can be used to design coatings capable of changing the wetting properties of a specific substrate. Nanoporous matrices on solid supports may be used for solid-phase diagnostics or as a biologically active component in solid-phase therapy procedures. The dewetting patterns and stability of nanoporous matrices of XG deposited on silicon and mica has been reported in the literature^[76].

2. Food industry

Polysaccharides are widely used in the food industry as functional ingredients for rheological control of the aqueous phase. Many polysaccharides perform as simple thickeners. Such materials are low cost commodities, and in general the cheapest find greatest application. Of greatest application are those polysaccharides which are able to confer novel rheological properties to the aqueous phase. While thickened polysaccharide solutions are related to the properties of disordered polymer chains interacting by virtue of entanglements, the origin of rigid and weak gel properties is specific molecular association of the polymer chains. In recent years a good understanding of the relationship between polysaccharide structure and rheological functional properties has been developed. As a result it is now recognized that the biotechnological tailoring of polysaccharide structure can result in an optimization of functional properties. Xyloglucan is widely used in the food industry as a functional ingredient for rheological control of the aqueous phase^[77]. At low water activity, i.e. at sugar concentration >60%, it forms a gel just like pectin, and it can be used in making jams, jellies, marmalade and mayonnaise production. It has been used in confectioneries, and as a binder in pharmaceutical tablets, thickening sauces, ice cream dressings, in processed vegetables, stabilizers, gelling agents, ice crystal stabilizers and starch modifiers^[78]. It forms a gel over a wide pH range. Less sugar is needed to achieve the desired gel strength than in corresponding pectin gels. The gels exhibit only a low syneresis phenomenon^[79]. A study on gelling behavior of polyose isolated from tamarind kernel powder (TKP) by alcohol extraction vis-a-vis pectin showed that 2% polyose from TKP is found to adequately substitute 1% pectin in ready-to-eat jelly formulations.

3. Paper industry

Use of XG in paper-making and replacing starch or galactomannan is of commercial importance due to its availability in abundance^[80]. Lately this idea has been further investigated and xyloglucan has been tested as a wet end additive^[81]. The addition of xyloglucan to the pulp reduces the friction of the fibers and may thereby improve sheet formation^[82-85]. Paper coated with xyloglucan in a spray application showed improved mechanical strength^[86]. XG can substitute starch in many adhesive applications, and as a binder in particle board, corrugated board and books^[82,87-88].

4. Textile industry

The chief use of the tamarind seeds lies in the manufacturing of textile sizing powder. It is widely used in sizing jute and cotton yarns. It is only half as costly as starch^[89,90]. The lowest grade tamarind kernel powder goes in textile sizing. It is also sometimes blended with other polysaccharides, in printing of polyester with disperse dyes and the results are reasonably good. However, it is unsuitable in printing cotton with vat dyes, due to the formation of insoluble complexes with dyes. It is also unsuitable in cotton printing with fiber reactive dyes. Anionic derivatives of XG have been shown to offer some advantages over regular XG in print paste thickeners. Adducts of XG with polyacrylic acid are useful in textile printing^[91]. Several patents on XG based materials for printing processes, fabric detergents and conditioning agents, enzymatic stone washing of denim, anti-wrinkling property for cellulosic fabrics, and dye antiredeposition agents have been obtained and information is available on the web^[92-98].

5. Others

5.1. As a biotic pesticide

A substance with elicitor activity may be used as a biotic pesticide. xyloglucan-oligoaccharide has elicitor activity and is notably useful as an agent for inducing a phytoalexin^[99]. This application of a xyloglucan-oligoaccharide to a plant can be carried out by the following routes—mixing a xyloglucan oligosaccharides into the soil where a plant is grown; a liquid fertilizer sprinkling a xyloglucan-oligoaccharide while a plant is grown; coating a seed of a plant with a xyloglucan-oligoaccharide by a procedure such as immersion, spraying, etc.; coating a plant itself, for example, whole vegetable or chopped vegetable, with a xyloglucan-oligoaccharide by a process such as immersion, spraying, etc.; preparing a capsule of a synthetic seed by way of

mixing an adventive embryo of a plant with a xyloglucan oligasaccharide, and, if necessary, with added nutrients and coating the resulting mixture with a water-soluble polymer such as sodium alginate, etc. Induction of a phytoalexin by applying a xyloglucan-oligoaccharide to a plant as mentioned above results in reduction of withering caused by pathogens. Accordingly, the growth of the plant can be promoted, and the freshness of a crop such as a vegetable can be maintained during transportation and storage.

5.2. As a surfactant

A novel class of non-ionic, carbohydrate-based surfactant has been synthesized from the plant polysaccharide xyloglucan. Enzymatic hydrolysis of xyloglucan yields a series of well defined, highly branched oligosaccharides that, following reductive amination, are readily conjugated with fatty acids bearing C8 to C18 chains under mild conditions. Several compounds from this new group of surfactants, especially those with C14 and C16 chains, are found to be useful for the extraction of membrane-bound enzyme markers from different plant cell compartments in catalytically active form^[100].

5.3. As a drilling fluid

Organic polymers are commonly used to control the rheology and filtrate loss required for water-based drilling fluids. An ecologically-friendly water-based drilling fluid was developed by studying the rheological behavior of XG and polyanionic cellulose on bentonite water suspensions. The drilling fluid that was developed has better rheological properties and fluid loss control which are required for optimum performance of oil well drilling. In addition, the drilling fluid filtrate exhibits minimum formation damage on sandstone cores^[101].

5.4. As a flocculant

Xyloglucan showed a good flocculation performance and has been studied for the removal of vat and direct dyes^[102]. Flocculation, using XG for sulfate and phosphate removal, was shown to be a simple and efficient treatment from economic and technical points of view^[103]. Sedimentation of clay slurry has been studied using tamarind seed kernel powder (TSKP). Experiments with chemical grade starch and its blends with TSKP were compared for their performance with that of potash alum for sedimentation of the clay slurry. TSKP offers faster sedimentation in the falling rate zone. Thus TSKP and its blends are potentially attractive environmentally benign flocculants^[104].

5.5. Xyloglucan helping in tannase formation

Tamarind seed powder obtained after removing the fruit pulp from tamarind fruit pods has been tested for the production of tannase under solid-state fermentation using *Aspergillus niger*. Tannase is an enzyme that catalyzes the hydrolysis of tannic acid to gallic acid, and is found in cultures of *Aspergillus* and *Penicillium*. The fungal strain grows on the substrate without any pretreatment. Results from the study are promising for economic utilization and value addition of this important agro-residue, which is abundantly available in many tropical and subtropical countries^[105].

Conflicts of interest:

There are no conflicts of interest.

REFERENCES

1. Phani Kumar GK, Gangarao Battu, Kotha NS, Lova Raju. 2011. Isolation and Evaluation of Tamarind Seed Polysaccharide being used as Polymer in Pharmaceutical Dosage Forms. Research Journal of Pharmaceutical, Biological and Chemical Science, 2(2):274.
2. Mayumi Shirakawa, Kazuhiko Yamatoya. 2003. Xyloglucan : Its Structure and Function. Foods Food Ingredients J. Jpn,208(11):2003
3. Mounika.S, Narayanan.V, Sarath Chandiran.I, Manasa.V, Sushma.S, Mahita T, Pavani . 2011. D. Pharmaceutical View of Tamarind Gum. The Pharma Professionals,1(2).
4. Anamika S, Shikha A. 2012. Solubility Enhancement Potential of Tamarind Seed Polysaccharide as Pharmaceutical Excipient. International Journal of Pharmaceutical & Biological Archives, 3(3):456-459.
5. Avachat AM, Dash RR, Shrotriya SN. 2011. Recent investigations of plant based natural gums, mucilages and resins in novel drug delivery systems. Ind J Pharm Edu Res, 45:86- 99.
6. Joshny J., Kanchalochana SN, Rajalakshmi G, Vedha Hari. 2012. Tamarind seed polysaccharide: A promising natural excipient for pharmaceuticals. International Journal of Green Pharmacy, 6(4):270-78

7. Kulkarni D, Dwivedi AK, Singh S. 1998. Performance evaluation of tamarind seed polyose as a binder and in sustained release formulations of low drug loading. *Indian J Pharma Sci*,1: 50-3.
8. Mishra MU, Khandare JN. 2007. Tamarind seed polysaccharides: biodegradable polymer for colonic drug delivery. Second International Conference and Indo-Canadian Satellite Symposium on Pharmaceutical Science, Technology, Practice and Natural Products, Conference Chronicle. *DDS*, 35, 206.
9. Hilken J, Ligtenberg MJ, Vos HL, Litvinov SV. 1992. Cell membrane-associated mucins and their adhesion modulating property. *Trends Biochem Sci*, 17:359-63.
10. Ghelardi E, Tavanti A, Celandroni F, Lupetti A, Blandizzi C, Boldrini E, et al. 2000. Effect of a novel mucoadhesive polysaccharide obtained from tamarind seeds on the intraocular penetration of gentamicin and ofloxacin in rabbits. *J Antimicrob Chemother*, 46:831-4.
11. Kulkarni D, Ddwivedi DK, Sarin JPS, Singh S. 1997. Tamarind seed polyose: A potential polysaccharide for sustained release of verapamil hydrochloride as a model drug. *Indian J Pharm Sci*, 59:1-7.
12. Giriraj T, Kulkarni K, Gawthamarajan. 2005. Development of controlled release spheroids using natural polysaccharides as release modifier. *Drug Deliv*, 12:201-6.
13. Ugwoke MI, Verbeke N, Kinget R. 2001. The biopharmaceutical aspects of nasal mucoadhesive drug delivery. *J. Pharm. Pharmacol*,53:3-21.
14. Kumar A, Garg T, Sarma GS, Rath G, Goyal AK. 2015. Optimization of combinational intranasal drug delivery. *Eur. J. Pharm. Sci*,70:140-151.
15. Courrier HM, Butz N, Vandamme TF. 2002. Pulmonary Drug Delivery systems: recent developments and prospects. *Crit. Rev. Ther. Drug Carrier Syst.*,19:425-498.
16. Patton JS, Platz RM. 1992. Routes of delivery: Case studies:(2) Pulmonary delivery of peptides and proteins for systemic action. *Adv. Drug Deliv. Rev.*, 8:179-196.
17. Bell J, Newman S. 2007. The rejuvenated pressurized metered dose inhaler. *Expert Opin. Drug Deliv.*,4(3):215-234.
18. Mahajan HS, Gundare SA. 2014. Preparation, characterization and pulmonary pharmacokinetics of xyloglucan microspheres as dry powder inhalation. *Carbohydr. Polym.*,102:529-536.
19. Hoogdalem E. van , de Boer AG, Breimer DD. Pharmacokinetics of rectal drug administration, part ii. Clinical applications of peripherally acting drugs, and conclusions. *Clin. Pharmacokinet.* 1991;21(2): 110-128.
20. Miyazaki, S., Suisha, F., Kawasaki, N., Shirakawa, M., Yamatoya, K., and Attwood, D. 1998. Thermally reversible xyloglucan gels as vehicles for rectal drug delivery. *J. Control. Rel.*, 56, 75-83.
21. Consuelo ID, Falson F, Guy RH, Jacques Y. 2007. Ex vivo evaluation of bioadhesive films for buccal delivery of fentanyl. *J Control Release*,122: 135-140.
22. Morales JO, McConville JT. 2011. Manufacture and characterization of mucoadhesive buccal films. *Eur. J. Pharm. Biopharm.*,77:187-199.
23. Vasantha PV, Puratchikody A, Mathew ST, Balaraman AK. 2011. Development and characterization of Eudragit based mucoadhesive buccal patches of salbutamol sulfate *Saudi Pharm. J.*,19(4):207-214.
24. Morales JO, McConville JT. 2011. *Eur. J. Pharm. Biopharm.*,77:187-199.
25. Avachat AM, Gujar KN, Wagh KV. 2013. *Carbohydr. Polym.*,91:537-542.
26. Miyazaki S, Ishitani M, Takahashi A, Shimoyama T, Itoh K, Attwood D. 2011. *Biol. Pharm. Bull.*,34:164-166.
27. Miyazaki S, Takahashi A, Itoh K, Ishitani M, Dairaku M, Togashi M. 2009. *Drug Dev. Ind. Pharm.*,35:780-787.
28. Listgarten MA. J. 1987. *Periodontal Res.*,22:172-178.
29. Vyas SP, Sihorkar V, Mishra V. 2000. *J. Clin. Pharm. Ther.*,25:21-42.
30. Svensson P, Petersen JK, Svensson H.1994. *Anesth. Prog.*,41:35-39.
31. Malamed SF, Sykes P, Kubota Y, Matsuura H, Lipp M. 1992. *Pain Control Dent.*,1:11-24.
32. Estafan DJ. 1998. *Gen. Dent.*,46:600-603.
33. Pandit AP, Pol VV, Kulkarni VS. 2016. Xyloglucan based in situ gel of lidocaine HCl for the treatment of periodontists. *J Pharm.*, 2016:1-9. .
34. Hagiwara A, Takahashi T, Lee R, Ueda T, Takeda M, Itoh T. 1987. *Cancer*,59:245-251.
35. Sasaki M, Ogita M. *Jpn. 1980. J. Cancer Chemother.*,7:1421-1426.
36. Miyazaki S, Ohkawa Y, Takada M, Attwood D. 1992. *Chem. Pharm. Bull.*,40:2224-2226.
37. Suisha F, Kawasaki N, Miyazaki S, Shirakawa M, Yamatoya K, Sasaki MD.1998. *Int. J. Pharm.*,172:27-32.
39. Miyazaki S, Tobiyama T, Takada M, Attwood D. 1995. *J. Pharm. Pharmacol.*,47:455-457.
40. Lee BJ, Lee TS, Cha BJ, Kim SH, Kim WB. 1997. *Int. J. Pharm.*,159:105-114.
41. Shin SC, Cho CW, Choi HK. 1999. *Drug Dev. Ind. Pharm.*,25:273-278.
42. Shin SC, Cho CW, Choi HK, Oh IJ. 2000. *Int. J. Pharm.*,193:213-218.
43. Miyazaki S, Suisha F, Kawasaki N, Shirakawa M, Yamatoya K, Attwood D. 1998. *J. Control Release*, 56:75-83.
44. Suisha F, Kawasaki N, Miyazaki S, Shirakawa M, Yamatoya K, Sasaki M, Attwood D. 1998. *Int. J. Pharm.*,172:27-32.
45. Miyazaki S, Suzuki S, Kawasaki N, Endo K, Takahashi A, Attwood D. 2001. *Int. J. Pharm.*,229:29-36.
46. Miyazaki S, Kawasaki N, Endo K, Attwood D. 2001. *J. Pharm. Pharmacol.*,53: 1185-1191.
47. Takahashi A, Suzuki S, Kawasaki N, Kubo W, Miyazaki S, Loebenberg R, Bachynsky J, Attwood D. 2002. *Int. J. Pharm.*,246:179-186.
48. Booth C, Attwood D. 2000. *Macromol. Rapid Commun.*,21:501.
49. Yuguchi Y, Urakawa H, Kajiwara K, Shirakawa M, Yamatoya K. 2017. Proceedings of the International Workshop on Green Polymers- Re-evaluation of Natural Polymers, in: H.T. Adishesha, S.T. Sudirjo, P.R. Panggabean, J. Arda, C.W. Soetrono (Eds.), Indonesian Polymer Association, 2001, pp. 253.
50. Ghelardi E, Tavanti A, Davini P, Celandroni F, Salvetti S, Parisio E, et al. 2004. A mucoadhesive polymer extracted from Tamarind seed improves the intraocular penetration and efficacy of Rofloxacin in Topical treatment at Experimental Bacterial Keratitis. *Antimicro Agents Chem.*,48: 3396-401.
51. R.Deveswaran et.al. 2009. Design and Characterization of Diclofenac sodium tablets containing Tamarind seed polysaccharide as Release retardant. *International Journal of PharmTech Research*, 1(2):191-195

52. Sumathi S and Ray AR. 2002. Release behavior of drugs from tamarind seed polysaccharides tablets. *J Pharm Pharm Sci*, 5(1):12-18.
53. Kulkarni D *et al.* 1998. Performance evaluation of tamarind seed polyose as a binder and in sustained release formulations of low drug loading. *J Pharm Pharm Sci.*,5(1):50-53.
54. Sougata Jana *et al.* 2010. Development and Evaluation of Epichlorohydrin Cross-linked Mucoadhesive Patches of Tamarind Seed Polysaccharide for Buccal Application. *IJPSDR*, 2(3):193-198.
55. Bhavin Patel *et al.* 2009. Evaluation of Tamarind Seed Polysaccharide (TSP) as a Mucoadhesive and sustained release component of nifedipine buccoadhesive tablet & Comparison with HPMC and Na CMC. *International Journal of PharmTech Research*, 1(3):404-410.
56. Rao PS, Ghosh TP, Krishna S. 1946. *J. Sci. Ind. Res. (India)*, 4:705.
57. Sano M, Miyata E, Tamano S, Hagiwara A, Ito N and Shirai T. 1996. *Food Chem. Toxicol.*,34:463.
58. Bungalassi S, Panichi L, Saettone MF, Jacobsen J and Rassing MR. 1996. *Int. J. Pharm.*,1:133.
59. Kulkarni D, Dwivedi DK, Sarin JPS and Singh S.1997. *Int. J. Pharm. Sci.*, 1:59.
60. Hensel A, Meier K. 1999. *Planta Med.*, 65(5): 395.
61. Strickland FM, Kuchel JM, Halliday GM. 2004. *Cutis*, 74:24.
62. Strickland FM, Sun Y, Darvill A, Eberhard S, Pauly M, Albersheim P. 2001. *J. Invest. Dermatol*, 116(1): 62.
63. Strickland FM, Darvill A, Albersheim P, Eberhard S, Pauly M and Pelley RP. 1999. *Photochem. Photobiol*, 69(2):141.
64. Kuchel JM, Barnetson RSC, Zhuang L, Strickland FM, Pelley RP and Halliday GM. 2005. *Lett. Drug Des. Discovery*, 2(2):165.
65. Mastromarino P, Petruzzello R, Macchia S, Rieti S, Nicoletti R, Orsi N. 1997. *J. Antimicrob. Chemother*, 39(3):339
66. Sinibaldi L, Pietropaolo V, Goldoni P, Di Taranto C and Orsi N. 1992. *J. Chemother*, 4(1):16.
67. Coviello T, Matricardi P and Alhaique F. 2006. *Exp. Opin. Drug Delivery*,3(3):395.
68. Aspinall GO. 1982. *The Polysaccharides*. Academic Press, New York.
69. Kardosova A, Machova E. 2006. *Fitoterapia*, 77:367.
70. Yu Cao, Isao Ikeda. 2009. *Int. J. Biol. Macromol.*, 45:231.
71. US Patent 6294190 September 2001.
72. Saito Y, Ogawa A, Sumii K, Umeki M, Yamamoto K, Ikegami S. 2003. *Proceedings of 57th Annual Meeting of Jpn. Soc. Nutr. Food Sci*, 292.
73. Hartemink R, Van Laere KMJ, Mertens AKC. 1996. *Anaerobe*, 2(4):223.
74. Makino C, Misaki A.1992. *J. Nutr. Sci. Vitaminol*, 38(4):391.
75. Yamatoya K, Shirakawa M, Kuwano K, Suzuki J, Baba O. 1996. *Macromolecular Symposia Japanese-German Seminar On Polysaccharides*,120, 231.
76. Tunland BC, Meyer D. 2002. *Comprehensive Reviews in Food Science and Food Safety*, 3:73.
77. Lubambo AF, Lucyszyn N, Kleinc JJ, Schreiner WH, Camargo PC, Sierakowski MR. 2009. *Colloids Surf B*, 70:174.
78. Iain CMD. 1989. *Industrial Polysaccharide*. *Pure Appl. Chem*,61(7):1315.
79. Shirakawa M, Yamatoya K, Nishinari K. 1998. *Food Hydrocolloids*, 12(1):25.
80. Schieberle P, Belitz HD, Grosch W. 2004. *Food Chemistry*. Springer, p.315.
81. Shankaracharya NB. 1998. *J. Food Sci. Tech.*,35:193
82. Christiernin M, Henriksson G, Lindstrom ME, Brumer H, Teeri TT, Lindstrom T, Laine J. Nord. 2003. *Pulp Pap. Res. J*, 18:182.
83. Brumer H, Zhou Q, Baumann MJ, Carlsson K, Teeri TT.2004. *J. Am. Chem. Soc.*, 126:5715.
84. Zhou Q, Baumann MJ, Brumer H, Teeri TT. *Carbohydr. Polym.*,63:449.
85. Stiernstedt J, Brumer H, Zhou Q, Teeri TT, Rutland MW. 2006. *Biomacromolecules*,7:2147.
86. Ahrenstedt L, Oksanen A, Salminen K, Brumer H. 2008. *Holzforchung*, 62(1):8.
87. Veluraja K, Ayyalnarayanasubburaj S, Paulraj AJ. 1997. *Carbohydr. Polym.*,34(4):377.
88. Lima DU, Oliveira RC, Buckeridge MS. 2003. *Carbohydr. Polym.*,52:367.
89. Rao PS, Srivastava HC. 1973. *Industrial Gums*. In: Whistler RL (ed). 2nd ed. New York:Academic Press, p. 369-411.
90. Shankaracharya NB. 1998. *J. Food Sci. Tech.*,35:193.
91. Abo-Shosha MH, Ibrahim NA, Allam E, El-Zairy E. 2008. *Carbohydr. Polym.*,74(2): 241.
92. US Patent 5594485 January 1997.
93. US Patent 6225462 May 2001 fabric detergent and conditioning agent.
94. US Patent 5914443 June 1999 enzymatic stone wash of denim.
95. US Patent 5968813 October 1999 anti wrinkling property for cellulosic fabrics.
96. US Patent 5885306 March 1999.
97. US Patent 5631684 May 1997.
98. US Patent 5635970 June 1997.
99. <http://www.wikipatents.com/5602111.html>
100. Greffe L, Bessueille L, Bulone V, Brumer H. 2004. *Glycobiology*,15(4):437.
101. Mahto V, Sharma VP. 2004. *J. Pet. Sci. Eng.*,45(1-2):123.
102. Mishra A, Bajpai M. 2006. *Bioresour. Technol.*,97:1055.
103. Mishra A, Bajpai M. 2006. *Colloid Polym Sci.*,284:443.
104. Chakrabarti S, Chaudhuri B, Bhattacharjee S, Dutta BK. 2008. *Bioresour. Technol.*,99(8):3313.
105. Sabu A, Pandey A, Daud MJ, Szakacs G.2005. *Bioresour. Technol.*, 96(11):1223.